-continued

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Glu Glu Glu Gly Gly Gly Glu
1               5


<210> SEQ ID NO 279
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: ARTIFICIAL
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: 1
<223> OTHER INFORMATION: optionally linked to side-chain carbonyl group
      of a para-acetyl-phenylalanine residue of a modified relaxin
      polypeptide
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: 6
<223> OTHER INFORMATION: gamma carbon optionally linked to a half-life
      extending moiety such as C13-CH3

<400> SEQUENCE: 279

Gly Gly Gly Gly Ser Glu
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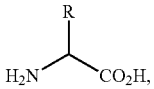
What is claimed is:

1. A method of treating a cardiovascular disease in a human subject with cardiovascular disease, comprising administering to said human subject an effective amount of a modified relaxin polypeptide comprising a non-naturally encoded amino acid, wherein:

(a) the modified relaxin polypeptide comprises the relaxin A chain polypeptide of SEQ ID NO: 4 and the relaxin B chain polypeptide of SEQ ID NO: 5 or SEQ ID NO: 6, substituted with a non-naturally encoded amino acid at A chain residue 1, and having zero, one, or two additional amino acid changes in said relaxin A chain and having zero, one, or two additional amino acid changes in said relaxin B chain, wherein each of said amino acid changes is independently a substitution, insertion or deletion;

(b) said non-naturally encoded amino acid has the structure:



wherein the R group is any substituent other than the side chain found in alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine or valine; and

(c) said non-naturally encoded amino acid is linked to a pharmacokinetic enhancer comprising a peptide component having between 4 and 8 amino acids and a half-life extending moiety comprising a fatty acid of Formula I:

-Cn-COOH (Formula I)

wherein n is between 12 and 16, wherein said peptide component comprises Glu^{γ}.

2. The method of claim **1**, wherein said non-naturally encoded amino acid comprises a carbonyl group, an aminooxy group, a hydrazide group, a hydrazine group, a semicarbazide group, an azide group, or an alkyne group.

3. The method of claim **1**, wherein said non-naturally encoded amino acid comprises a phenylalanine derivative, and/or wherein said non-naturally encoded amino acid is directly linked to said peptide component.

4. The method of claim **1**, wherein said non-naturally encoded amino acid is linked to said pharmacokinetic enhancer through an oxime linkage or triazole linkage.

5. The method of claim **1**, wherein said relaxin A chain polypeptide comprises SEQ ID NO: 35, and said relaxin B chain polypeptide comprises SEQ ID NO: 6.

6. The method of claim **1**, wherein said peptide component comprises Glu, GGGGS-Glu^{γ} (SEQ ID NO: 139), DRDDRD (SEQ ID NO: 102), KKKKKK-Glu^{γ} (SEQ ID NO: 103), GGGEEE-Glu^{γ} (SEQ ID NO: 105), EEEGGG-Glu^{γ} (SEQ ID NO: 106), KKKGGG-Glu^{γ} (SEQ ID NO: 107), GGGKKK-Glu^{γ} (SEQ ID NO: 109), Sar-Sar-Sar-Sar-Ser-Glu^{γ} (SEQ ID NO: 112), Sar-Sar-Sar-Glu-Glu-Glu^{γ} (SEQ ID NO: 113), KSGGSGG-Glu^{γ} (SEQ ID NO: 117), dKdKdKdKdKdK-Glu^{γ} (SEQ ID NO: 120), EEEGGG-$dGlu^{\gamma}$ (SEQ ID NO: 128), EGGGGSK-Glu^{γ} (SEQ ID NO: 130), EEEEEE-Glu^{γ} (SEQ ID NO: 131), KK-Glu^{γ} (SEQ ID NO: 140), KGPKGP-Glu^{γ} (SEQ ID NO: 146), SGGGS-Glu^{γ} (SEQ ID NO: 147), KGGGS-Glu^{γ} (SEQ ID NO: 148), KGGGSE-Glu^{γ} (SEQ ID NO: 149), GSPGSP-Glu^{γ} (SEQ ID NO: 150), GGGGP-Glu^{γ} (SEQ ID NO: 151), EGGS-Glu^{γ} (SEQ ID NO: 152), EGGGP-Glu^{γ} (SEQ ID NO: 153), KGPGSE-Glu^{γ} (SEQ ID NO: 154), Spermine-Glu^{γ}, or KKGGS-Glu^{γ} (SEQ ID NO: 156).

7. The method of claim **1**, wherein the relaxin polypeptide comprises the relaxin A chain polypeptide of SEQ ID NO: 4 and the relaxin B chain polypeptide of SEQ ID NO: 5 or SEQ ID NO: 6, substituted with a non-naturally encoded amino acid at A chain residue 1, wherein said non-naturally encoded amino acid is linked to said pharmacokinetic enhancer and said pharmacokinetic enhancer comprises the peptide component GGGGS-Glu^{γ} (SEQ ID NO: 139).